CONCLUSIONS. Three years of SLIT as an adjunct to pharmacotherapy in house dust mite–allergic children with asthma resulted in a reduction of the necessity for ICS usage along with improvement in lung functions.

REVIEWER COMMENTS. This study adds to the body of work defining SLIT as a modality that is capable of providing clear but modest benefit in the treatment of allergic airway disease. The primary focus was on evaluating the steroid-sparing effect of SLIT. Unfortunately, symptom scores and rescue-medication usage were not reported. There was a 31% drop-out rate after 3 years among the SLIT group, compared with 18% among the pharmacotherapy group. So, although there may be some compliance advantage in SLIT over injection immunotherapy, there are clearly still some adherence challenges. This study demonstrates that the addition of SLIT to standard pharmacotherapy can provide a significant decreases in ICS usage and modest increases in lung function over the course of 3 years of treatment.

Cutting Edge: Immunosuppressant as Adjuvant for Tolerogenic Immunization

PURPOSE OF THE STUDY. Immunosuppressive agents are used frequently for the treatment of allergy, autoimmune disease, and transplant rejection but are thought to provide only temporary benefit. The authors of this study sought to determine if dexamethasone, a glucocorticoid with potent immunosuppressive properties, could promote long-term antigen-specific tolerance when administered with a peptide immunogen.

METHODS. The authors used a model of delayed-type hypersensitivity (DTH) to hen ovalbumin by subcutaneously injecting ovalbumin twice during a 2-week interval into BALB/c mice. Mice with established DTH to ovalbumin were then immunized with an ovalbumin-derived MHCII-restricted peptide in the presence or absence of dexamethasone. All mice were retested for DTH at 2-week and 4- to 5-month time points after completion of immunization by injecting ovalbumin into the footpad and measuring the increase in footpad thickness. Blood-derived CD4+CD25+Foxp3+ regulatory T cells (Tregs) were quantitated by labeling peripheral white blood cells with carboxyfluorescein diacetate succinimidyl ester (CFSE), stimulating the cultures with ovalbumin peptide, and analyzing for CFSE dilution (indicating cell division). Dendritic cells (DCs) in draining lymph nodes were stained for Foxp3 and quantitated by flow cytometry. The primary findings were that dexamethasone significantly increased the percentage of peripheral blood-derived Tregs and Tregs were mainly CD4+CD25+Foxp3+ regulatory T cells (Tregs) and that the prophylactic effect of dexamethasone was mediated through a reduction in the number of DCs in the draining lymph nodes.

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Immunotherapy and Immunomodulation
Efficacy of Long-term Sublingual Immunotherapy as an Adjunct to Pharmacotherapy in House Dust Mite-Allergic Children With Asthma

PURPOSE OF THE STUDY. To evaluate the effect of 3 years of dust mite sublingual immunotherapy (SLIT) on clinical and laboratory outcome measurements.

STUDY POPULATION. This was a prospective study of 90 children aged 4 to 16 years who were followed for 4 years from the time of enrollment. Inclusion criteria were mild-to-moderate persistent asthma requiring an inhaled steroid, monosensitization to dust mite, and no previous history of immunotherapy.

METHODS. Participants were randomly assigned to treatment for 3 years with dust mite SLIT plus standard pharmacotherapy or pharmacotherapy alone. The prescribed SLIT solution consisted of 50% Dermatophagoides pteronyssinus and 50% Dermatophagoides farinae. Doses were increased gradually to a maintenance dose, which was taken 2 times per week. All participants were initially started on 800 µg/day of inhaled budesonide. Follow-up visits were performed every 2 to 3 months, at which times the inhaled corticosteroid (ICS) dose was decreased until either it was discontinued or the minimum dose allowing for control of symptoms was reached. Pulmonary-function testing was performed at each visit. Skin-prick testing to 15 aeroallergens and a serum total immunoglobulin E measurement were performed annually.

RESULTS. A total of 90 children were randomly assigned: 62 to SLIT plus pharmacotherapy and 28 to pharmacotherapy alone. There were 19 drop-outs (31%) in the SLIT group after 3 years compared with 5 (18%) in the pharmacotherapy group. The number of months per year in which the children required ICS, as well as mean dose per day of budesonide, was significantly lower in the SLIT group compared with pharmacotherapy group during all 3 years. By the end of the 3 years, 52.4% in the SLIT group versus 9.1% in the pharmacotherapy group were able to successfully discontinue ICSs for at least 6 months. Both forced expiratory volume in 1 second and forced expiratory flow, midexpiratory phase, were significantly increased from baseline in the SLIT group after 3 years, whereas the pharmacotherapy controls showed no change. Total immunoglobulin E levels were significantly decreased only in the SLIT group after 3 years. Finally, there were no serious adverse reactions during the study.

Blood-derived CD4+CD25+Foxp3+ regulatory T cells (Tregs) were quantitated by labeling peripheral white blood cells with carboxyfluorescein diacetate succinimidyl ester (CFSE), stimulating the cultures with ovalbumin peptide, and analyzing for CFSE dilution (indicating cell division). Dendritic cells (DCs) in draining lymph nodes were stained for Foxp3 and quantitated by flow cytometry. The primary findings were that dexamethasone significantly increased the percentage of peripheral blood-derived Tregs and Tregs were mainly CD4+CD25+Foxp3+ regulatory T cells (Tregs) and that the prophylactic effect of dexamethasone was mediated through a reduction in the number of DCs in the draining lymph nodes.
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